Sponsor

Novartis

Generic Drug Name

vildagliptin

Therapeutic Area of Trial

Type 2 Diabetes Mellitus

Approved Indication

Galvus is indicated as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus (T2DM).

- **as monotherapy**
- **in dual combination**
  - with metformin, when diet, exercise and metformin alone do not result in adequate glycemic control.
  - with a sulphonylurea (SU), when diet, exercise and a SU alone do not result in adequate glycemic control.
  - with a thiazolidinedione (TZD) when diet, exercise and a TZD do not result in adequate glycemic control.
- **in triple combination**
  - with a sulphonylurea and metformin when diet and exercise plus dual therapy with these agents do not provide adequate glycemic control.

Galvus is also indicated in combination with insulin (with or without metformin) when diet, exercise and a stable dose of insulin do not result in adequate glycemic control (in Europe).
Galvus is also indicated as initial combination therapy with metformin in patients with T2DM whose diabetes is not adequately controlled by diet and exercise alone.

Approved indications may vary by country.

Galvus is currently approved in more than 100 countries across Europe, Asia Pacific, Africa, Middle East and Latin America including Australia, Argentina, Brazil, Chile, China, Columbia, Costa Rica, Denmark, Dominican Republic, Ecuador, El Salvador, Egypt, EU, France, Honduras, Hong Kong, Germany, Greece, Guatemala, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Kuwait, Liechtenstein, Malaysia, Malta, Mexico, Netherlands, Nicaragua, Norway, Peru, Philippines, Poland, Qatar, Russia, Saudi Arabia, Singapore, South Africa, South Korea, Spain, Switzerland, Taiwan, Thailand, Turkey, UAE, United Kingdom, Venezuela.

Protocol Number

CLAF237A23150

Title

A multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of 24 weeks treatment with vildagliptin in type 2 diabetes mellitus patients ≥ 70 years (drug-naïve or inadequately controlled on oral agents)

Phase of Development

Phase III

Study Start/End Dates

22 Dec 2010 to 14 Mar 2012

Study Design/Methodology

This was a multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of 24 weeks treatment with vildagliptin versus placebo in patients ≥70 years with T2DM who were either drug-naive or have inadequately controlled HbA1c levels (≥7.0 and ≤10.0%) on stable doses of OADs for at least 12 weeks prior to screening. The dose of treatment for all patients was either vildagliptin 50mg bid or placebo (or vildagliptin 50mg qd or placebo qd for patients on background SU monotherapy). Patients on background therapy with SU plus another OAD received either vildaglipitin 50mg bid or placebo bid. An individualized 24-week HbA1c target for each of the patients was defined by the investigators based on the age of the patient, baseline HbA1c value, frailty status, and co-morbidities. The clinical judgment of the investigator and the local recommendations for glycemic targets were also considered.

Centres

60 centers in 7 countries: Belgium (7), Bulgaria (8), Finland (3), Germany (12), Slovakia (6), United Kingdom (5), Spain (4)

Publication

Outcome measures

Primary outcome measures(s)

• to evaluate the efficacy of vildagliptin as initial or add-on therapy in elderly patients with T2DM who are drug-naive or inadequately controlled with OADs by testing the hypothesis that the HbA1c reduction with vildagliptin is superior to that of placebo after 24 weeks of treatment.
• to evaluate the proportion of elderly patients with T2DM who are drug-naive or inadequately controlled with OADs by testing the hypothesis that the proportion of patients reaching their investigator-defined individual target HbA1c while being treated with vildagliptin is superior to that of placebo after 24 weeks of treatment.

Secondary outcome measures(s)

• To evaluate the safety and tolerability of vildagliptin as initial or add-on therapy in elderly patients with T2DM who are drug-naive or inadequately controlled with OADs during 24 weeks.
• To evaluate the efficacy of vildagliptin as initial or add-on therapy in elderly patients with T2DM who are drug-naive or inadequately controlled with OAD by testing the hypothesis that the FPG reduction with vildagliptin is superior to that of placebo after 24 weeks of treatment.
• To assess the responder rates of vildagliptin, as compared to placebo, in elderly patients with T2DM who are drug-naive or inadequately controlled with OADs.

Test Product (s), Dose(s), and Mode(s) of Administration

The test drugs (vildagliptin 50 mg tablets or matching placebo) were provided as tablets which were to be taken twice daily for patient on OADs as background anti-diabetic treatment and once daily for patients on background SU monotherapy.

Statistical Methods

The test for the superiority of vildagliptin (50mg bid and 50mg qd combined) to placebo for the effect of reducing HbA1c after 24 weeks of treatment, was based on the following null hypotheses and onesided alternative hypotheses at α level of 0.6%: H0: $\rho Vilda \geq \rho Placebo$ versus Ha: $\rho Vilda < \rho Placebo$ where ρs are the mean change from baseline at Week 24 endpoint in HbA1c in the treatment group indicated.

ANCOVA model including terms for treatment, baseline HbA1c (centered by subtracting the overall mean baseline HbA1c of all treatment groups), background OAD strata and pooled center was used to compare the treatment effect.

The test for the superiority of vildagliptin (50mg bid and 50mg qd combined) to placebo for proportion of patients who reached their individual target HbA1c after 24 weeks of treatment, was based on the following null hypotheses and one-sided alternative hypotheses at an α-level of 1.9%:

H0: ρvilda(1-ρplacebo)/ρplacebo(1-ρvilda) ≤ 1
Ha: ρvilda (1-ρplacebo)/ρplacebo(1-ρvilda) >1

where ρ is the proportion of patients who reach their individual target HbA1c at Week 24 endpoint in HbA1c in the treatment group indicated.

The percentage of responders (proportion of patients who reach their individual target HbA1c) at 24 week was analyzed by a logistic regression model including the terms treatment, baseline HbA1c (centered by subtracting the overall mean baseline HbA1c of all treatment groups), background OAD strata, and pooled center to compare the treatment effect.

A testing strategy was used to maintain an overall 2.5% level for the two primary one-sided hypotheses. The analyses of the primary efficacy variables using the Full analysis set were the primary basis of conclusion. Sensitivity analyses based on the PP set were also performed to assess the robustness of the conclusion. The same testing procedure as for the FAS analysis was used.

For the secondary efficacy variables, the change from baseline in FPG at study endpoint was analyzed using ANCOVA model in the same way as the primary efficacy variable of HbA1c. The percentage of patients meeting predefined responder criteria based on HbA1c targets at study endpoint was computed and compared using a Cochran-Mantel-Haenszel chi-square test, with background OAD as a stratification variable Chi-square test, for the FAS.

Demographic and background data as well as safety and efficacy data were summarized by treatment group.

Study Population: Key Inclusion/Exclusion Criteria and Demographics

1. Male and female
2. >70 years old
3. T2DM inadequately controlled (HbA1c ≥7% and ≤10.0%)
4. OAD regimen that may include an SU or with SU monotherapy or in drug naïve patients.
5. Confirmed diagnosis of T2DM by standard criteria.
6. Treatment with oral anti-diabetic therapy, on stable dose for at least 12 weeks prior to the Visit 1. OADs that are allowed for this study are metformin, SU, thiazolidinediones, α-glucosidase inhibitors, and meglitinides, used either as monotherapy or in combination.
7. Drug-naive patients diagnosed at least 12 weeks prior to Visit 1 (drug-naive is defined as no treatment with OADs for at least 12 weeks prior to Visit 1 and no treatment with OADs for > 3 consecutive months at any time in the past).
8. HbA1c of ≥ 7% and ≤10.0% by central laboratory at Visit 1 and assessed by the investigator to be inadequately controlled.

9. Body Mass Index (BMI) 19-45 kg/m2 at Visit 1.

Exclusion criteria:

1. FPG ≥270mg/dL (15mmol/L) at Visit 1.

2. use of any of the prohibited medications as assessed at Visit 1.

3. a history or evidence of any of the following:
   a. acute metabolic conditions within the past 6 months.
   b. current diagnosis of congestive heart failure (NYHA III or IV).
   c. myocardial infarction within the past 6 months.
   d. coronary artery bypass surgery or percutaneous coronary intervention within the past 6 months.
   e. stroke or similar neurologic events within the past 6 months
   f. unstable angina within the past 3 months.
   g. sustained and clinically relevant ventricular arrhythmia
   h. active substance abuse, alcohol abuse within the past 2 years.
   i. type 1 diabetes
   j. malignancy of an organ system treated or untreated, within the past 5 years, regardless of whether there is evidence of
      local recurrence or metastases.
   k. hepatic disorder defined as:
      - acute or chronic liver disease, evidence of hepatitis, cirrhosis or portal hypertension.
      - history of imaging abnormalities that suggest liver disease, such as portal hypertension, capsule scalloping, cirrhosis.
   l. acute infections which may affect blood glucose control within the past 4 weeks.

4. any of the following significant laboratory abnormalities as assessed at Visit 1:
   a. clinically significant increase or reduction in thyroid stimulating hormone (TSH) outside of the normal range.
   b. clinically significant renal dysfunction: glomerular filtration rate (GFR)
   c. alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 2x upper limit of normal (ULN) at Visit 1
   d. total bilirubin > 2x ULN and/or direct bilirubin > 1x ULN
   e. positive Hepatitis B surface antigen (HBsAg).
   f. positive Hepatitis C virus (HCV) antibody test (anti-HCV).
   g. elevated fasting triglycerides (TGs) >500mg/dL (5.65mmol/L).
   h. clinically significant laboratory abnormalities

5. any of the following electrocardiographic abnormalities at Visit 1:
   a. second or third degree atrio-ventricular block without a pacemaker.
   b. long QT syndrome or QTc >500ms.
   c. clinically significant electrocardiogram (ECG) abnormalities

6. previous or current participation in any vildagliptin clinical study.

7. history of hypersensitivity to DPP-4 inhibitors.

8. concurrent medical condition that may interfere with the interpretation of efficacy and safety data during the study.

9. donation of blood or significant blood loss equaling to at least one unit of blood within the past 2 weeks of start of study
10. potentially unreliable, inability to comply with the study procedures or medications, and/or judged by the investigator to be unsuitable for the study.
11. use of an investigative drug within 30 days or 5 half-lives of the drug, whichever is longer. No additional exclusions were to be applied by the investigator, in order to ensure that the study population will be representative of all eligible patients.

Other protocol defined inclusion/exclusion criteria applied.

Participant Flow (Randomized set)

Disposition Reason	Vildagliptin* N=139 n (%)	Placebo N=139 n (%)	Total N=278 n (%)
Completed	131 (94.2)	131 (94.2)	262 (94.2)
Discontinued	8 (5.8)	8 (5.8)	16 (5.8)
Adverse Event(s)	5 (3.6)	2 (1.4)	7 (2.5)
Abnormal laboratory value(s)	0	0	0
Abnormal test procedure result(s)	0	0	0
Unsatisfactory therapeutic effect	0	2 (1.4)	2 (0.7)
Subject's condition no longer requires study drug	0	0	0
Subject withdrew consent	0	3 (2.2)	3 (1.1)
Lost to follow-up	1 (0.7)	0	1 (0.4)
Administrative problems	1 (0.7)	0	1 (0.4)
Death	1 (0.7)	1 (0.7)	2 (0.7)
Protocol deviation	0	0	0

*Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy)

Baseline Characteristics (Randomized set)

Demographic variable	Vildagliptin* N=139	Placebo N=139	Total N=278
Age (years)			
n	139	139	278
Mean (SD)	75.1 (4.29)	74.4 (4.03)	74.8 (4.17)
Min- Max	70.0- 97.0	70.0- 89.0	70.0-97.0
Median	75.0	73.0	74.0
Age group			
< 75 yrs	68 (48.9)	86 (61.9)	154 (55.4)
>= 75 yrs	71 (51.1)	53 (38.1)	124 (44.6)
Sex			
Male	73 (52.5)	53 (38.1)	126 (45.3)
Female	66 (47.5)	86 (61.9)	152 (54.7)
Race			
Caucasian	135 (97.1)	134 (96.4)	269 (96.8)
Other	4 (2.9)	5 (3.6)	9 (3.2)
Height (cm)			
n	139	139	278
Mean (SD)	165.5 (9.41)	162.6 (9.40)	164.0 (9.50)
Min -Max	140.0- 187.0	136.0- 188.0	136.0- 188.0
Median	166.0	161.0	164.0
Body weight (kg)			
n	139	139	278
Mean (SD)	79.8 (12.35)	80.6 (13.55)	80.2 (12.95)
Min - Max	52.5- 126.0	52.0- 115.8	52.0-126.0
Median	79.5	80.2	80.0

BMI (kg/m**2)			
n	139	139	278
Mean (SD)	29.1 (3.78)	30.5 (4.75)	29.8 (4.34)
Min	22.0	22.1	22.0
Median	28.6	29.7	29.1
Max	39.0	44.7	44.7
BMI group			
<30 (kg/m**2)	87 (62.6)	73 (52.5)	160 (57.6)
>=30 (kg/m**2)	52 (37.4)	66 (47.5)	118 (42.4)
>=35 (kg/m**2)	11 (7.9)	26 (18.7)	37 (13.3)

Background Characteristic	**Vildagliptin* N=139**	**Placebo N=139**	**Total N=278**
HbA_{1c} (percent)			
n	139	139	278
Mean (SD)	7.9 (0.76)	7.9 (0.69)	7.9 (0.72)
Min - Max	6.6- 10.3	6.6- 10.1	6.6- 10.3
Median	7.8	7.8	7.8
HbA_{1c} group (percent)			
<=8	85 (61.2)	88 (63.3)	173 (62.2)
>8	54 (38.8)	51 (36.7)	105 (37.8)
<=9	127 (91.4)	130 (93.5)	257 (92.4)
>9	12 (8.6)	9 (6.5)	21 (7.6)
FPG (mmol/L)			
n	139	139	278
Mean (SD)	9.6 (2.28)	9.9 (2.12)	9.7 (2.20)
Min - Max	4.6- 17.5	4.9-16.4	4.6- 17.5
Median	9.2	9.7	9.5
Duration of Type 2 Diabetes (years)			
n	139	139	278
Mean (SD)	12.2 (7.92)	10.6 (6.93)	11.4 (7.47)
Min - Max	1.3- 35.0	0.3- 32.8	0.3-35.0
Median	10.1	9.2	9.9
GFR (MDRD) (mL/min/1.73m**2)			
Normal (>80)	34 (24.5)	31 (22.3)	65 (23.4)
Mild (>=50 - <=80)	86 (61.9)	87 (62.6)	173 (62.2)
Moderate (>=30 - <50)	19 (13.7)	21 (15.1)	40 (14.4)
Severe (<30)	0	0	0
Is subject a current smoker?			
Yes	6 (4.3)	5 (3.6)	11 (4.0)
No	133 (95.7)	134 (96.4)	267 (96.0)
Frailty status			
Yes	12 (8.6)	14 (10.1)	26 (9.4)
No	126 (90.6)	123 (88.5)	249 (89.6)
Missing	1 (0.7)	2 (1.4)	3 (1.1)

*Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).

Outcome measures

Primary Outcome Result(s)

ANCOVA results for change in HbA_{1c} (%) from baseline to endpoint by treatment (Full analysis set (FAS) and Per Protocol (PP) set)

			Adjusted	Difference in adjusted mean change		
		Baseline	mean change	(Vildagliptin - Placebo)		
Treatment	n	mean (SE)	(SE)	mean (SE)	(98.8% CI)	P Value
FAS						
Vildagliptin	137	7.92 (0.06)	-0.86 (0.12)	-0.57 (0.10)	(-0.81,-0.33)	<0.001 *
Placebo	137	7.91 (0.06)	-0.28 (0.12)			
PP set						
Vildagliptin	128	7.91 (0.07)	-0.86 (0.13)	-0.58 (0.10)	(-0.83,-0.33)	<0.001 *
Placebo	130	7.91 (0.06)	-0.29 (0.12)			

- Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Baseline is the measurement obtained on Day 1, or on sample obtained on an earlier visit (scheduled or unscheduled) which was closest to Day 1, if Day 1 measurement is missing. Endpoint is defined as the final available post-baseline assessment obtained at any visit (scheduled or unscheduled), prior to or at the start of rescue medication use, up to final scheduled study visit. “n” is the number of patients with observations at both baseline and endpoint. Adjusted means and the associated standard errors (SE), confidence intervals (CI), and p values were from an ANCOVA model containing terms for treatment, centered HbA_{1c} baseline, background OAD strata, and pooled centers.
- * indicates statistical significance at the one-sided 0.6% level.

Logistic regression results for the number (%) of patients who reached the investigator-defined HbA_{1c} target at endpoint (Full analysis set and Per Protocol set)

				Treatment difference (Vildagliptin - Placebo)		
	n	Number of responders	Proportion of responders (%)	Odds ratio	96.2% CI of odds ratio	p-value
FAS						
Vildagliptin	137	72	52.6	3.16	(1.81, 5.52)	<0.001 *
Placebo	137	37	27.0			
PP set						
Vildagliptin	128	69	53.9	3.23	(1.82, 5.76)	<0.001 *
Placebo	130	36	27.7			

- Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Endpoint is defined as the final available post-baseline assessment obtained at any visit (scheduled or unscheduled), prior to or at the start of rescue medication use, up to the final scheduled study visit.
- n is the number of patients with observations at both baseline and endpoint.
- Odds ratios, associated confidence interval and p values are calculated from a logistic regression model containing terms for treatment, centered baseline HbA1c, background OAD strata, and pooled centers.
- * indicates statistical significance at one-sided 1.9% level;** indicates statistical significance at one-sided 2.5% level.

Secondary Outcome Result(s)

ANCOVA results for change in FPG (mmol/L) from baseline to endpoint by treatment (Full analysis set and Per Protocol set)

			Adjusted	Difference in adjusted mean change		
		Baseline	mean change	(Vildagliptin* - Placebo)		
Treatment	**n**	**mean (SE)**	**(SE)**	**mean (SE)**	**(95% CI)**	**P Value**
FAS						
Vildagliptin	137	9.58 (0.20)	-1.34 (0.27)	-0.87 (0.21)	(-1.28,-0.46)	<0.001 *
Placebo	137	9.86 (0.18)	-0.47 (0.26)			
PP set						
Vildagliptin	128	9.60 (0.21)	-1.28 (0.27)	-0.90 (0.21)	(-1.31,-0.48)	<0.001 *
Placebo	130	9.80 (0.19)	-0.38 (0.26)			

- *Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Baseline is the measurement obtained on Day 1, or on sample obtained on an earlier visit (scheduled or unscheduled) which was closest to Day 1, if Day 1 measurement is missing.
- Endpoint is defined as the final available post-baseline assessment obtained at any visit (scheduled or unscheduled), prior to or at the start of rescue medication use, up to final scheduled study visit.
- n is the number of patients with observations at both baseline and endpoint. Adjusted means and the associated standard errors (SE), confidence intervals (CI), and p values were from an ANCOVA model containing terms for treatment, centered HbA1c baseline, background OAD strata, and pooled centers.
- * indicates statistical significance at the one-sided 2.5% level.

Number (%) of patients who responded at endpoint (based on reduction in HbA_{1c}) (Full analysis set)

	Vildagliptin* N=137 n (%)	**Placebo N=137 n (%)**	**p-value [1]**
N'	137 (100)	137 (100)	
Responder Criterion			
At least one criterion met	104 (75.9)	59 (43.1)	<0.001 *
HbA_{1c} <= 7.5%	104 (75.9)	59 (43.1)	<0.001 *
HbA_{1c} < 7%	61 (44.5)	27 (19.7)	<0.001 *
HbA_{1c} < 7% in patients with baseline HbA_{1c} <= 8%	50 (60.2)	20 (23.3)	<0.001 *

- *Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Baseline is the measurement obtained on Day 1 or on sample obtained on an earlier visit (scheduled or unscheduled) which was closest to Day 1, if Day 1 measurement is missing.
- Endpoint is defined as the final available post-baseline assessment obtained at any visit (scheduled or unscheduled), prior to or at the start of rescue medication use, up to final scheduled study visit.

[1] Cochran-Mantel-Haenszel chi-square test for Vildagliptin vs. Placebo. Significance will be tested at the 5% level.

N' = number of patients with both baseline and endpoint HbA_{1c} measurements, which is used as the denominator unless specified otherwise.

Safety Results

Adverse Events by System Organ Class

Primary system organ class	Vildagliptin N=139 n (%)	Placebo N=139 n (%)
Any primary system organ class	66 (47.5)	63 (45.3)
Blood and lymphatic system disorders	3 (2.2)	1 (0.7)
Cardiac disorders	7 (5.0)	4 (2.9)
Ear and labyrinth disorders	1 (0.7)	3 (2.2)
Endocrine disorders	0	1 (0.7)
Eye disorders	5 (3.6)	0
Gastrointestinal disorders	12 (8.6)	9 (6.5)
General disorders and administration site conditions	13 (9.4)	8 (5.8)
Infections and infestations	18 (12.9)	24 (17.3)
Injury, poisoning and procedural complications	4 (2.9)	4 (2.9)
Investigations	2 (1.4)	3 (2.2)
Metabolism and nutrition disorders	5 (3.6)	5 (3.6)
Musculoskeletal and connective tissue disorders	12 (8.6)	14 (10.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	2 (1.4)
Nervous system disorders	21 (15.1)	12 (8.6)
Psychiatric disorders	1 (0.7)	1 (0.7)
Renal and urinary disorders	0	3 (2.2)
Reproductive system and breast disorders	3 (2.2)	0
Respiratory, thoracic and mediastinal disorders	3 (2.2)	11 (7.9)
Skin and subcutaneous tissue disorders	11 (7.9)	10 (7.2)
Surgical and medical procedures	1 (0.7)	0
Vascular disorders	6 (4.3)	6 (4.3)

- Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Primary system organ classes are presented alphabetically.
- A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category for that treatment.
- A patient with multiple adverse events within a primary system organ class is counted only once in the total row.

Most Frequently Reported AEs Overall by Preferred Term n (%)

Number (%) of patients reporting common AEs (greater than or equal to 2% in any group) by preferred term (safety set)

Preferred term	Vildagliptin* N=139 n (%)	Placebo N=139 n (%)
Dizziness	11 (7.9)	3 (2.2)
Headache	8 (5.8)	4 (2.9)
Nasopharyngitis	7 (5.0)	7 (5.0)
Hyperhidrosis	5 (3.6)	6 (4.3)
Constipation	4 (2.9)	1 (0.7)
Hunger	4 (2.9)	2 (1.4)
Urinary tract infection	4 (2.9)	5 (3.6)
Anaemia	3 (2.2)	1 (0.7)
Arthralgia	3 (2.2)	0
Diarrhoea	3 (2.2)	4 (2.9)
Hot flush	3 (2.2)	1 (0.7)
Hypoglycaemia	3 (2.2)	1 (0.7)
Influenza	3 (2.2)	2 (1.4)
Oedema peripheral	3 (2.2)	1 (0.7)
Pain in extremity	3 (2.2)	6 (4.3)
Tremor	3 (2.2)	4 (2.9)
Back pain	2 (1.4)	4 (2.9)
Cough	0	3 (2.2)
Upper respiratory tract infection	0	3 (2.2)

- Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- A patient with multiple occurrences of an AE under one treatment is counted only once in the AE category.
- Preferred terms are sorted by descending order of incidence in the Vildagliptin group.

Serious Adverse Events and Deaths

Number (%) of patients with serious or clinically significant AEs during the double-blind period (safety set)

Event category	Vildagliptin* 50mg	Placebo
Deaths	1 (0.7)	1 (0.7)
SAEs	8 (5.8)	5 (3.6)
Discontinuation due to AEs	6 (4.3)	3 (2.2)
AEs causing dose adjustment or study drug interruption	1 (0.7)	2 (1.4)
Clinically significant CCV AEs	5 (3.6)	3 (2.2)
Clinically significant hepatic AEs	0	0
Clinically significant SVEM AEs	1 (0.7)	1 (0.7)
Clinically significant Breast cancer AEs	0	0
AEs of predefined risk	21 (15.1)	24 (17.3)

- *Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).

Other Relevant Findings

Number of patients experiencing hypoglycemic events during the randomized double-blind period by event profile and treatment (safety set)

	Vildagliptin* N=139 n (%)	**Placebo N=139 n (%)**
Number (%) of patients with at least one hypoglycemic event	3 (2.2)	1 (0.7)
Number (%) of patients with		
one hypoglycemic event	1 (0.7)	1 (0.7)
two hypoglycemic events	0	0
>2 hypoglycemic events	2 (1.4)	0
Number (%) of patients who discontinued due to hypoglycemic events	1 (0.7)	0
Number (%) of patients with grade 2 hypoglycemic events	0	0
Number (%) of patients with suspected grade 2 hypoglycemic events	0	0

- *Vildagliptin = Vildagliptin 50 mg bid (or 50 mg qd for patients on SU monotherapy).
- Hypoglycemic events are defined as a) symptoms suggestive of hypoglycemia, where the patient is able to initiate self-treatment and plasma glucose measurement is < 3.1 mmol/L (grade 1), b) symptoms suggestive of hypoglycemia, where the patient is unable to initiate self-treatment and plasma glucose measurement is < 3.1 mmol/L (grade 2), c) symptoms suggestive of hypoglycemia, where the patient is unable to initiate self-treatment and no plasma glucose measurement is available (suspected grade 2).

Date of Clinical Trial Report

9 OCT 2012

Date Inclusion on Novartis Clinical Trial Results Database

19 DEC 2012

Date of Latest Update